Clinical trial results:
Quadratus lumborum 3 block (QLB3) for laparoscopic colorectal surgery: A double blind, prospective randomized placebo-controlled trial.

Summary

EudraCT number	2019-002304-40
Trial protocol	BE
Global end of trial date	24 July 2022

Results information

Result version number	v1 (current)
This version publication date	19 August 2023
First version publication date	19 August 2023

Trial information

Trial identification

Sponsor protocol code	SC05-2019

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Leuven
Sponsor organisation address	Herestraat 49, Leuven, Belgium,
Public contact	anesthesiology research, University hospitals Leuven, christel.huygens@uzleuven.be
Scientific contact	anesthesiology research, University hospitals Leuven, christel.huygens@uzleuven.be

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 December 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 July 2022
Global end of trial reached?	Yes
Global end of trial date	24 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The goal of this study is to improve pain management, minimize the need for postoperative opioids and to facilitate postoperative recovery after laparoscopic colorectal surgery. Our hypothesis is that a bilateral single shot QLB 3 block with 30mL ropivacaine 0,375% on each side is associated with a reduction in postoperative morphine consumption as compared to normal saline 0,9%. Superiority of the QLB 3 block will be defined as a 30% reduction in the cumulative 24-hour morphine consumption post-surgery.

Protection of trial subjects:

Postoperatively, all patients received multimodal intravenous analgesia including paracetamol, ketorolac and patient-controlled analgesia (PCIA) with morphine.
Rescue medication consisted of clonidine, metamizole and ketamine.
Patiënts received PCIA up unto 24 hours after surgery. Paracetamol and morphine was given after stopping PCIA.
Follow-up till discharge and evaluation of pain scores were standardised.-surgery.

Background therapy:

Irrespective of any group allocation every patient received 0.1-0.2 mg/kg morphine at extubation and end surgery.
At transfer PACU after surgery all patients received the PCIA and with evaluation of painscores extra clinical bolus of Morphine 2 mg was given if NRS > 4
All standard multimodal analgesia was given (ketorolac, paracetamol)

Evidence for comparator:

No big multicenter trails were conducted yet to evaluate the QLB in laparoscopic colorectal surgery.
A few small trials however detected advantage in caesarian section and kidney surgery.
Given the anatomic basis and the possibility to give analgesia over a larger portion of the abdominal wall, investigation seems mandatory

Actual start date of recruitment	16 September 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 150
Worldwide total number of subjects	150
EEA total number of subjects	150

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	84
From 65 to 84 years	66
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

From november 29, 2019 till 21st of July 2022 a total of 173 patients were screened in Leuven and 158 in Kortrijk. Eventually 150 patients were enrolled, 100 in Leuven and 50 in Kortrijk.

Pre-assignment

Screening details:

all consecutive patients between 18 and 75 years of age scheduled for elective laparoscopic colorectal surgery were screened for potential enrolment. Inclusion criteria were American Society of Anesthesiologists (ASA) classification of physical status I-III, a body mass index (BMI) ≤ 35, and the ability to understand the use of PCIA

Period 1

Period 1 title	Surgery (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Blinding implementation details:

Patients were randomized using a computer-generated permuted block randomization sequence (variable block size with 1:1 allocation). Enclosing assignments in opaque, sequentially numbered, sealed envelopes ensured allocation concealment. Prior to anesthesia, upon arrival in the preoperative holding area, the randomization envelope was opened and medication was prepared by an independent member of the research team not involved in the study or subject's care. Syringes labeled as trial medication

Arms

Are arms mutually exclusive?	Yes
Arm title	Intervention

Arm description:

The bilateral AQLB was placed before induction of anesthesia. The patient was first positioned in the left and then in the right lateral decubitus position.
A total of 60 ml was placed either 2x30 ml on each side ropivacaine 0,375%.

Arm type	Placebo
Investigational medicinal product name	Ropivacaine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use

Dosage and administration details:

A total of 60 ml was placed either 2x30 ml on each side ropivacaine 0,375% at QLB interfascial plane

Arm title	Control

Arm description:

The bilateral AQLB was placed before induction of anesthesia. The patient was first positioned in the left and then in the right lateral decubitus position.
A total of 60 ml was placed 2x30ml normal saline 0,9% at the QLB fascia plane

Arm type	Placebo
Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use

Dosage and administration details:
2x30ml normal saline 0,9% at QLB interfascial plane

Number of subjects in period 1	Intervention	Control
Started	75	75
Completed	75	75

Baseline characteristics

Reporting groups	
Reporting group title	Intervention
Reporting group description:	
The bilateral AQLB was placed before induction of anesthesia. The patient was first positioned in the left and then in the right lateral decubitus position. A total of 60 ml was placed either 2x30 ml on each side ropivacaine 0,375%.	
Reporting group title	Control
Reporting group description:	
The bilateral AQLB was placed before induction of anesthesia. The patient was first positioned in the left and then in the right lateral decubitus position. A total of 60 ml was placed 2x30ml normal saline 0,9% at the QLB fascia plane	

Reporting group values	Intervention	Control	Total
Number of subjects	75	75	150
Age categorical			
Adult ages were included			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	46	49	95
From 65-84 years	29	26	55
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	37	32	69
Male	38	43	81

Subject analysis sets	
Subject analysis set title	Control
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Analysing QLB on postoperative pain	
Subject analysis set title	Intervention
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The coefficient of variation (CV) in postoperative morphine consumption was assumed to equal 0.7 and derived from own data.[6] To have 80% power to show a 30% reduction in the 24-h consumption in the ropivacaine group versus the placebo group using a two-sided test for a ratio of means (with alpha= 5%), at least 51 patients per group were needed (i.e., 102 patients in total). The total number of subjects was increased to 128 to have also at least 80% power in a secondary analysis to detect an effect of ropivacaine within the subgroup of patients with a BMI≤30 (this group was expected to constitute 80% of the total sample). In order to compensate for possible dropouts we included 150 patients in total.	

Reporting group values	Control	Intervention	
Number of subjects	75	75	
Age categorical			
Adult ages were included			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	46	49	
From 65-84 years	29	26	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	37	32	
Male	40	43	

End points

End points reporting groups

Reporting group title	Intervention

Reporting group description:

The bilateral AQLB was placed before induction of anesthesia. The patient was first positioned in the left and then in the right lateral decubitus position.
A total of 60 ml was placed either 2x30 ml on each side ropivacaine 0,375%.

Reporting group title	Control

Reporting group description:

The bilateral AQLB was placed before induction of anesthesia. The patient was first positioned in the left and then in the right lateral decubitus position.
A total of 60 ml was placed 2x30ml normal saline 0,9% at the QLB fascia plane

Subject analysis set title	Control
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Analysing QLB on postoperative pain

Subject analysis set title	Intervention
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The coefficient of variation (CV) in postoperative morphine consumption was assumed to equal 0.7 and derived from own data.[6] To have 80% power to show a 30% reduction in the 24-h consumption in the ropivacaine group versus the placebo group using a two-sided test for a ratio of means (with alpha= 5%), at least 51 patients per group were needed (i.e., 102 patients in total). The total number of subjects was increased to 128 to have also at least 80% power in a secondary analysis to detect an effect of ropivacaine within the subgroup of patients with a BMI≤30 (this group was expected to constitute 80% of the total sample). In order to compensate for possible dropouts we included 150 patients in total.

Primary: Morphine consumption 24 hours

End point title	Morphine consumption 24 hours

End point description:

Primary outcome was the cumulative morphine consumption during the first 24 hours after extubation. Secondary outcomes included severity of pain, presence/extent of sensory block, the incidence of post-operative nausea and vomiting as well as recovery and hospital length of stay. We also investigated the need for and dose of rescue analgesia. Safety outcomes included the incidence of adverse events.

End point type	Primary

End point timeframe:

Morphine during the first 24 hours using PCIA

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	75		
Units: mg				
median (inter-quartile range (Q1-Q3))	28.6 (9 to 39)	28.4 (12 to 39.1)		

Statistical analyses

Statistical analysis title	Primary outcome
Comparison groups	Intervention v Control
Number of subjects included in analysis	150
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.05
Method	t-test, 2-sided

Notes:

[1] - For the primary outcome, a two-sided independent t-test was used for the difference as well as for for the ratio of the geometric means to compare the 24-h cumulative morphine intake between both groups. A 95% confidence interval for the difference and for the ratio of the geometric means was reported. Secondary outcomes were compared using Fisher's exact test for proportions, and Mann-Whitney U tests were used when data were measured on a ratio or ordinal level. P-values smaller than 0.05 were

Secondary: Pain scores

End point title	Pain scores

End point description:

End point type	Secondary

End point timeframe:

NRS pain scores during 4 hour time frame in PACU and the wards untill discharge

End point values	Intervention	Control	Control	Intervention
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	75	75	75	75
Units: NRV units	75	75	75	75

Statistical analyses

No statistical analyses for this end point

Secondary: Safety

End point title	Safety

End point description:

End point type	Secondary

End point timeframe:

All adverse events and safety points (nausea, redo surgery, bleeding, systemic toxicity)

End point values	Intervention	Control	Control	Intervention
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	75	75	75	75
Units: Complication events	41	40	41	40

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From enrollment until discharge of the patient	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25

Reporting groups	
Reporting group title	Intervention
Reporting group description:	
Before induction of anesthesia, patients received a bilateral AQLB in the left and right lateral decubitus position under ultrasound guidance 30 ml of either ropivacaine 0.375% (n=75)	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Intervention	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 75 (0.00%)	0 / 75 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Intervention	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 75 (26.67%)	20 / 75 (26.67%)	
Gastrointestinal disorders			
postopertaive nausea, vomiting and ileus			
subjects affected / exposed	20 / 75 (26.67%)	20 / 75 (26.67%)	
occurrences (all)	20	20	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 March 2022	Amendment 1 and 2 Adding extra center (Kortrijk) Increasing age Adjusting inclusion criteria (ifo Liver and kidney function)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported